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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/388,899	09/02/1999	BEREND HOUWEN	10690/T/B/A	4619

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EXAMINER	
GABEL, GAILENE	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 02/04/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/388,899	HOUWEN ET AL.	
	Examiner	Art Unit	
	Gailene R. Gabel	1641	

--The MAILING DATE f this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 07 January 2002 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☒ The period for reply expires 6 months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1.☒ A Notice of Appeal was filed on *07 January 2002*. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2.☐ The proposed amendment(s) will not be entered because:

(a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

(b) ☐ they raise the issue of new matter (see Note below);

(c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

(d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____.

3.☐ Applicant's reply has overcome the following rejection(s): _____.

4.☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5.☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See Continuation Sheet*.

6.☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7.☐ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: *NONE*.

Claim(s) objected to: *NONE*.

Claim(s) rejected: *1-11*.

Claim(s) withdrawn from consideration: *NONE*.

8.☐ The proposed drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9.☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10.☐ Other: _____

Continuation of 5. does NOT place the application in condition for allowance because: claims 1-10 remain anticipated by the prior art of record and claim 11 remains obvious over the art of record .

Request for Reconsideration

1. Applicant's request for reconsideration and response filed 1/7/02 in Paper No. 10 is acknowledged. Currently, claims 1-11 are pending and under examination.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 1-10 stand rejected under 35 U.S.C. 102(b) as being anticipated by Bowen et al. (Laboratory Hematology, 1997) for reason of record.

3. Claims 1-10 stand rejected under 35 U.S.C. 102(b) as being anticipated by Loken et al. (EP 0317516) for reason of record.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claim 11 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Bowen et al. (Laboratory Hematology, 1997) in view of McCarthy et al. (Journal of Immunological Methods, 1993) for reason of record.

Response to Arguments

5. Applicant's arguments filed 1/7/02 have been fully considered but they are not persuasive.

A) Applicant argues that Examiner has not established a prima facie case under 35 USC §102 anticipatory rejection and requests the Office to point out where each and every fact in the claim is disclosed in the Bowen reference.

In response, Bowen teaches classifying and counting leucocytes as required by the claimed invention. Specifically, Bowen teaches adding to a hematological sample (bone marrow sample) a fluorescence labeled antibody specific to leucocytes (Tri-color conjugated CD45 antibody), a fluorescence labeled antibody specific to at least one

type of neutrophilic cell, and a fluorescence labeled antibody specific to an immature granulocyte (FITC conjugated anti-CD16 or PE-conjugated anti-CD11b) to stain leucocytic cells in the hematological sample then analyzing the cells using flow cytometry (see page 294, column 1, first and second full paragraphs). Bowen teaches analyzing leucocytic cell populations in the hematological sample by obtaining five data parameters including fluorescence intensity and side/orthogonal light scatter. Bowen defines groups or populations on the basis of intensity of scattered light and intensity of fluorescence. Specifically, Bowen defines granulocytic cells on the basis of intensity of scattered light and intensity of fluorescence of the first fluorescence labeled antibody specific to leucocytes (Tri-color conjugated CD45 antibody), i.e. granulocytes including all granulocytic stages and promyelocytes have distinctly greater orthogonal scatter than other leucocyte populations (see page 292, column 2, first full paragraph and page 294, column 1, third full paragraph and column 2, first full paragraph). Bowen defines neutrophil cells on the basis of intensity of fluorescence of the first fluorescence labeled antibody specific to leucocytes and intensity of fluorescence from the second or third-fluorescence labeled antibody (FITC conjugated anti-CD16 or PE-conjugated anti-CD11b). Bowen also confirmed that peripheral blood neutrophil populations within varying maturation levels (promyelocytes, myelocytes, metamyelocytes, and band cells) are quantified within the CD11b and CD16 regions because both CD16 and CD 11b normally increase during the maturation of granulocytes from promyelocytic stage to segmented neutrophil stage (see page 294, column 2). Bowen defines and classifies neutrophilic cells into different degrees of maturity on the basis of intensity of the

fluorescence from the second fluorescence-labeled antibody and the intensity from the third fluorescence-labeled antibody in page 292, column 2, first full paragraph (CD11b expression appears earlier and prior to the expression of CD16: CD11b increases during early to late myelocyte stages and CD16 expression appears during metamyelocytic stage and increases during maturation through band and segmented stages and therefore, anti-CD16 antibodies are more useful in defining granulocytes in later maturation stages than CD11b) (see page 296, column 2). Bowen teaches lysing erythrocytes with Ortho Lyse before prior to analysis of the samples (see page 294, column 1, lines 2-5). For at least these teachings by Bowen, it is said that claims 1-10 are anticipated by Bowen et al.

B) Applicant argues that Examiner has not established a prima facie case under 35 USC §102 anticipatory rejection because Loken fails to teach or identify each and every element of claim 1.

In response, Loken discloses a method and kit for classifying and counting leucocytes comprising the requirements set forth by the claimed invention. Specifically, Loken teaches adding to a hematological sample (bone marrow sample) a fluorescence labeled monoclonal antibody specific to leucocytes (fluorochrome labeled CD45 antibody), a fluorescence labeled antibody specific to at least one type of neutrophilic cell, and a fluorescence labeled antibody specific to an immature granulocyte (fluorochrome, i.e. FITC and PE, labeled monoclonal anti-CD16 and anti-CD11b antibodies) to stain leucocytic cells in the hematological sample then analyzing the cells

using flow cytometry (see column 5). Loken defines groups or populations on the basis of intensity of scattered light and intensity of fluorescence. Specifically, Loken defines granulocytic cells from other leucocytes on the basis of intensity of side angle light scatter which provides a measure of cellular granularity in leucocytic cells (see column 4, lines 4-24). Loken uses anti-CD45, anti-CD16, and anti-CD11b antibodies to distinguish neutrophilic cells and between granulocytic myeloid maturation stages (see column 7, lines 31-34, column 8, lines 35-52). See also claims 1-4 and 6 of Loken reference. For at least these teachings by Loken, it is said that claims 1-10 are anticipated by Loken et al.

C) Applicant further argues that Loken does not disclose distinguishing granulocytes from eosinophils.

In response, it is noted that the features upon which applicant relies (i.e., distinguishing granulocytes from eosinophils) are not recited in the rejected claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Alternatively, eosinophils are granulocytes (containing granules) which should inherently be separated and distinguished in the early myelocytic stages with the rest of the neutrophilic cell population.

D) Applicant argues that McCarthy teaches away from removal of erythrocytes prior to staining and that available procedures affect the sample and are not desirable.

Therefore, McCarthy lacks the requisite suggestion or motivation to obtain the claimed invention.

In response, McCarthy is incorporated with Bowen, only for teaching that removal of erythrocytes prior to being labeled for flow cytometric analysis is known in the art, i.e. Ficoll-Hypaque and dextran sedimentation, specifically described by McCarthy, constitute an obvious modification of procedures routinely varied in the art, and which has not been described as being critical to the practice of the invention.

6. Applicant's arguments filed 1/7/02 have been fully considered but they are not persuasive.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (703) 305-0807. The examiner can normally be reached on Monday to Thursday, 6:30 AM - 4:00 PM and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (703) 308-3399. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

grg
February 1, 2002

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP ~~1800~~ 1641